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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/692,084	08/08/96	RODRIGUEZ M	1199 1 001 C

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DAVID A JACKSON
KLAUBER AND JACKSON
411 HACKENSACK AVENUE
HACKENSACK NJ 07601

EXAMINER	
DUFFY,P	
ART UNIT	**PAPER NUMBER**
1645	32

DATE MAILED: 05/07/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/692,084	Rodriguez, et al
Examiner	**Group Art Unit**
DUFFY	1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on CPA & Amendment E filed 4/20/00 & 5/16/00 respectively

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1-21 is/are pending in the application.

Of the above claim(s) 5-8, 15-17 is/are withdrawn from consideration.

☒ Claim(s) 20, 21 is/are allowed.

☒ Claim(s) 1-4, 9-14, 19 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1-21 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachm nt(s)

☐ Information Disclosure Statem nt(s), PTO-1449, Paper No(s). _____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Acti n Summary

Continued Prosecution Application

1. The request filed on 4-20-00 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/692,084 is acceptable and a CPA has been established. An action on the CPA follows.

2. The amendment filed 5-16-00 has been entered into the record. Claims 1-4, 9-14 and 19-21 are under examination. This application contains claims 5-8 and 15-18 drawn to an invention nonelected with traverse in Paper No. 7.

3. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

4. The rejection of claim 19 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 5,591,629 this is a double patenting rejection is maintained inasmuch as applicant has acknowledged this rejection (see top of page 3 of response) but has failed to traverse the rejection is withdrawn based on Applicants' amendment to the claim.

5. The rejection of claims 1-4, 9 and 11-14 under 35 U.S.C. 102(b) as being anticipated by Miller et al (J. Neurosci., 14:6230-6238, 1994) is maintained for reasons made of record in Paper No. 9, mailed 10-2-97 is withdrawn based on Applicants' amendments to the claims.

Claim Rejections - 35 USC § 112

6. The rejection of claims 1-4, 9-14 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of stimulating

remyelination or treating a demyelinating disease in a mammal by administering to a mammal an effective amount of the monoclonal antibody A2B5 and stimulation of remyelination by administering to a mammal an effective amount of SCH 79.08, it does not reasonably provide enablement for, antibodies SCH 79.08, 01, 04, HNK-1, isolated or synthetic autoantibodies for treatment of a demyelinating disease or antibodies 01, 04, HNK-1, isolated or synthetic autoantibodies for stimulation of remyelination. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims is maintained for reasons made of record in Paper No. 9, mailed 10-2-97.

Applicants' arguments have been carefully considered but are not fully persuasive. With respect to antibodies 01, 04, HNK-1 and stimulation of remyleination, the only remaining issue is the public avialablity of the specific monoclonal antibody clones. with respect to both the method of stimulation of remyelination and treatment of demyelinating disease. As previously set forth,

> "...the specification recites the HNK-1 clone of monoclonal antibody, applicants are claiming the HNK-1 clone. Neither exhibit A nor exhibit B provides for the sale of the clone *HNK-1*. As to exhibit A, the anti-CD-57 antibodies for sale block the HNK-1 binding, but are not the clone HNK-1, and thus is not persuasive. As to exhibit B, again the antibody cited is "NK-1" and not "HNK-1" as is instantly claimed. Thus, it is not apparent that the clone referenced in the specification and claimed is the same clone which applicants indicates is for public sale. As to Exhibit C, the designation as a distributor is not an indication that the HNK-1 clone is publicly available with unrestricted access by these companies (i.e. for sale). Thus, applicants evidence does not establish the unrestricted publicly availability of the claimed antibody HNK-1. Applicants' have not established that the publicly available antibodies are identical to that monoclonal antibody claimed and cited in the specification as HNK-1. As to the O1 and O4 monoclonal antibodies. Applicants' evidence does not indicate the public availability of both of these specific monoclonal antibodies. The evidence of record (Exhibit F) Kettenmann et al

(Neruosci Lett, 1985, 54(2-3):195-9) teaches that eleven monoclonal antibodies 01-011 were made. However, this does not establish that these particular monoclonal antibodies are publicly available. Exhibit G of Roche Molecular Biochemicals USA establishes a clone 59 which also binds the 01 antigen. Applicants' have not established that clone 59 is identical to the monoclonal 01 antibody of the specification and art and thus have not established the public availability of the monoclonal 01 antibody of the specification. Exhibit G of Roche Molecular Biochemicals USA establishes a clone 81 which also binds the 04 antigen. Exhibit F of Chemicon International Inc. establishes the public availability of monoclonal antibody 345. Applicants' have not established that either clone 59 or MAB345 is identical to the monoclonal 04 antibody of the specification and thus have not established the public availability of the monoclonal 04 antibody of the specification.

Applicants' are claiming specific monoclonal antibodies, the evidence must demonstrate that the claimed monoclonal antibody of the specification is identical to that which is on sale. Deposits are required for specific antibodies because of the events of recombination and affinity maturation lead to unpredictable sequence changes. Thus, for reasons of record, the exact reproduction of a specific antibody is an unpredictable event. Therefore applicants' evidence must show that the antibodies which are publicly available are identical to that which is claimed (i.e. amino acid sequence, structure, and function). Applicants' have not yet met this burden the clones which are on sale are not the antibody 01, 04 or HNK-1 as claimed and recited in the specification. As to applicants' Exhibit G, exhibit G is not persuasive because it describes the use of isolated and purified polyclonal human IgG or IgM. It does not describe "isolated or synthetic autoantibodies". The art defines an autoantibody as an antibody which is capable of reaction with an antigen which is a normal constituent of the body. In no case has the evidence established that normal serum has autoantibodies as defined by the art. The pooled human IgG and IgM of Exhibit G are not equivalent to "isolated or synthetic autoantibodies". One could not make and use the instantly claimed isolated or synthetic autoantibodies" for reasons made of record. Evidence demonstrating isolation of pooled human IgG or IgM is not equivalent to that which is now claimed. Moreover, any of the starting materials, methods, procedures and starting materials are not provided for in the

specification. The use of pooled human IgG or IgM is not mentioned in the specification and therefore the reliance on methodology known to the art to isolate such is misplaced.

As to the deposit issues, it is noted that Applicants' are specifically claiming monoclonal antibody clones "O1" and "O4". They are not claiming any monoclonal that binds the "O1" or "O4" oligodendrocyte antigens. Applicants' have not provided deposit information for monoclonal antibody clones "O1" or "O4" as are specifically claimed. The monoclonal antibody clones "O1" or "O4" are specific clones produced by others, see for example Exhibit A of the response and amendment dated September 30, 1999, Kettenmann et al., Neuroscience Letters, 54(2-3):195-199, March 15, 1985 and Bastmeyer et al., Neuroscience Lett, 101(2):127-32, June 19, 1989. The references in the art provide for specific monoclonal antibody clones entitled "O1" or "O4". Applicants are claiming the use of monoclonal antibodies produced by these specific clones, not by other clones that bind the same antigen as the monoclonal antibodies specifically known to the art at monoclonal antibody clones "O1" or "O4". Applicants argue that the "O1" or "O4" antibodies of Roche that are publicly available were those used by applicants. The clones provided by Roche or Chemicon are not entitled "O1" or "O4" and therefore do not fulfill the public availability requirement. It is also not persuasive because the specification describes lists the "O1" and "O4" with other specific monoclonal antibody clones. Consequently, the only reasonable interpretation of the passage as set forth in the specification is that applicants intended monoclonal antibody clone "O1" or "O4" as described in the art. Applicants' specification does not direct one of skill in the art to either the Roche or Chemicon antibodies. The specification directs one to specific monoclonal antibodies "O1" and "O4" of the art and not to the Roche or Chemicon antibodies as asserted (see for example page 9, lines 4-10). Applicants' claims are directed to a specific exact clone. There is no evidence that the monoclonal antibody clones "O1" or "O4" of the prior art were obtained from Roche or

Chemicon. Since the claims are to a specific exact clone, it is that clone, not a similar one or one that binds the same antigen, producing that exactly identical antibody which is required to be deposited. Applicants' declaration is not persuasive to this point because it does not provide evidence that the publicly available monoclonal antibodies provided by Roche that bind the "O1" or "O4" antigen have the same exact structure as the monoclonal antibody clones "O1" or "O4" of the art. In regard to the isolated or synthetic autoantibodies, the polyclonal autoantibodies of the evidence are limited to human IgM and stimulation of remyelination and as such is not commensurate in scope with the claims.

Applicants again argue that "isolated or synthetic autoantibodies" are fully enabled by the specification and presents Exhibit H. This is not persuasive, the methodology used to produce the specific IgM germline antibody or the method of making polyclonal IgM or IgG is not contemplated or present in this specification. Applicants assertion that the knowledge to produce such is in the skill of the art is again not persuasive, the courts have held that:

> "However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It meas that the omission of minor detains does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material *or of any conditions under which a process can be carried out,* [emphasis added] undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research." (Genentech Inc. v. Novo Nordisk A/S Ltd., 42 USPQ2d 1001).

In the instant case there is no disclosure of how to make such isolated or synthetic autoantibodies in this specification as originally filed and the evidence presented is not

commensurate in scope with the claims. It is further noted that enablement must be established in the specification at the time of filing and is to be commensurate in scope with the stated claims (*In re Hogan and Banks*, 194 USPQ 527(1977). The specification does not teach that isolated polyclonal IgM and isolated polyclonal IgG are so useful and are equated with the instantly claimed isolated or synthetic autoantibodies. Moreover, as previously set forth, methods of making polyclonal antibodies are unpredictable and there is lot to lot variation.

The rejection is maintained for all the reasons made of record.

New Rejections

Claim Rejections - 35 USC § 112

7. Claims 1-4, 9-14 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 1, 9 and every claim dependent thereon, the claims are indefinite because they recite an improper Markush language. A Markush group must be closed. The current recitation of "or" in the claims is improper.

As to claims 4 and 13, the term "monoclonal antibody" lacks antecedent basis in the claim from which it depends.

8. Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Abo et al (J. Immunol., 127:1024-1029, 1981) or American Type Culture Collection Catalog, 1992, page 435.

Abo et al teach the monoclonal antibody HNK-1. As such the product claim is anticipated.

American Type Culture Collection Catalog, 1992, page 435 teaches the monoclonal antibody HNK-1 for sale with under restricted conditions. As such the claimed antibody is anticipated.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (f) he did not himself invent the subject matter sought to be patented.

10. Claim 19, as drawn to the HNK-1 antibody is rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

American Type Culture Collection catalog 1992, page 435, describes ATCC™ TIB 200 monoclonal antibody HNK-1 was deposited by T. Abo and C. Balch. In view of this evidence, it is clear that applicants were not the inventor of the recited HNK-1 antibody.

Status of Claims

11. Claims 20 and 21 are allowed. All other claims stand rejected.

Conclusion

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
April 23, 2001

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600